

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE
 in its capacity as elected Office

Date of mailing (day/month/year) 10 May 2001 (10.05.01)	
International application No. PCT/GB00/03291	Applicant's or agent's file reference RJW/LP5871900
International filing date (day/month/year) 24 August 2000 (24.08.00)	Priority date (day/month/year) 27 August 1999 (27.08.99)
Applicant THURSTON, David, Edwin et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 13 March 2001 (13.03.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Juan Cruz Telephone No.: (41-22) 338.83.38
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PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY EXAMINATION REPORT (PCT Rule 71.1)

To:

WATSON, Robert J.
MEWBURN ELLIS
York House
23 Kingsway
London WC2B 6HP
GRANDE BRETAGNE

RECEIVED
- 3 DEC 2001

Date of mailing (day/month/year)	30.11.2001
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Applicant's or agent's file reference RJW/LP5871900	IMPORTANT NOTIFICATION
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International application No. PCT/GB00/03291	International filing date (day/month/year) 24/08/2000	Priority date (day/month/year) 27/08/1999
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Applicant SPIROGEN LIMITED et al.

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary examination report and its annexes, if any, established on the international application.
2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.
3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.
4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary examination report. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

<p>Name and mailing address of the IPEA/</p> <div style="display: flex; align-items: center;"> <div> <p>European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465</p> </div> </div>	<p>Authorized officer</p> <p>Ambroa, J.R.</p> <p>Tel. +49 89 2399-8012</p>
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PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference RJW/LP5871900	<div style="display: flex; justify-content: space-between;"> <div>FOR FURTHER ACTION</div> <div>See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)</div> </div>	
International application No. PCT/GB00/03291	International filing date (<i>day/month/year</i>) 24/08/2000	Priority date (<i>day/month/year</i>) 27/08/1999
International Patent Classification (IPC) or national classification and IPC C07D209/60		
Applicant SPIROGEN LIMITED et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.

2. This REPORT consists of a total of 8 sheets, including this cover sheet.

☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 12 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☒ Certain defects in the international application
- VIII ☒ Certain observations on the international application

Date of submission of the demand 13/03/2001	Date of completion of this report 30.11.2001
Name and mailing address of the international preliminary examining authority: <div style="display: flex; align-items: center;"> <div> European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465 </div> </div>	Authorized officer Von Daacke, A Telephone No. +49 89 2399 8286



**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/03291

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):
Description, pages:

1-53 as originally filed

Claims, No.:

10 (part), 11, 12 as originally filed

1-9, 10 (part), with telefax of 20/11/2001
13-30

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
☐ the language of publication of the international application (under Rule 48.3(b)).
☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
☐ filed together with the international application in computer readable form.
☐ furnished subsequently to this Authority in written form.
☐ furnished subsequently to this Authority in computer readable form.
☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
☐ the claims, Nos.:
☐ the drawings, sheets:

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/GB00/03291

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):
(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

- ☐ the entire international application.
☒ claims Nos. 1-9,28.

because:

- ☒ the said international application, or the said claims Nos. 28 (Industrial Applicability) relate to the following subject matter which does not require an international preliminary examination (*specify*):
see separate sheet
- ☒ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. 1-9 are so unclear that no meaningful opinion could be formed (*specify*):
see separate sheet
- ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.
- ☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

- ☐ the written form has not been furnished or does not comply with the standard.
☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims 10-30
	No: Claims
Inventive step (IS)	Yes: Claims

**I. . . ERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/GB00/03291

	No:	Claims	10-30
Industrial applicability (IA)	Yes:	Claims	10-27, 29,30
	No:	Claims	

2. Citations and explanations
see separate sheet

VII. Certain defects in the international application

The following defects in the form or contents of the international application have been noted:
see separate sheet

VIII. Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:
see separate sheet

III NON-ESTABLISHMENT

1. Due to the use of the term 'combinatorial unit' the object of Claims 1-9 is completely unclear (Art. 6 PCT). It is in particular not clear whether it relates to individual compounds, a stochastic mixture thereof (random library) or a set of spatially separate individuals. Moreover, as the term is already used in Claim 10 for describing a diradical, it is lastly unclear whether it should alternatively refer only to diradical species.
2. Claim 28 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of this claim (Article 34(4)(a)(i) PCT).

V REASONED STATEMENT

1. PRIOR ART

The documents cited in the International Search Report

D1: WO 99 29642 A (THE SCRIPPS RESEARCH INSTITUTE) 17 June 1999 (1999-06-17)

D2: WO 98 11101 A (AUCKLAND DIVISION CANCER SOCIETY OF NEW ZEALAND INC.) 19 March 1998 (1998-03-19) cited in the application

D3: WO 97 07097 A (AUCKLAND DIVISION CANCER SOCIETY OF NEW ZEALAND INC.) 27 February 1997 (1997-02-27)

D4: WO 91 16324 A (THE UPJOHN COMPANY) 31 October 1991 (1991-10-31) have been considered for the examination procedure.

2. NOVELTY

The subject-matter of Claims 10-30 appears to be novel in view of D1-D4. (Article 33(2) PCT), mainly due to the fact that either combinatorial methods are not described in these documents or an amide linkage to the A-B containing ring is not described therein.

3. INVENTIVE STEP

The subject-matter of Claims 10-30 does not fulfil the requirements of Article 33(3) PCT for the following reasons.

As can be seen from the entire description, the core of the present application relates in the provision of libraries of different compound classes which all include the CPI unit according to structures A and B as described on page 2. Using the library technology including common screening methods it is suggested to discover biologically active compounds starting from the tool of free compounds II, II', IV, IV', VIII and X. The remaining compound groups are to be considered as 'precursor tools'.

The compound claims are formulated as usual Markush claims, i.e. 'Compounds of the formula xy, wherein..'. An inventive step for claims to chemical compounds may be acknowledged on the basis of an unexpected effect, property or use provided that essentially all the compounds covered by the claim possess this unexpected effect, property or use. As only several compounds of the former compound group (II, II' etc.) are expected to possess such an effect use or property, the technical problem underlying the present claims should be seen in the provision of new chemical compounds. Such a problem is to be regarded as obvious per se because it belongs to the routine work of a chemist to synthesize novel compounds. Under this aspect, an inventive step cannot be recognized for the compound claims.

The use of combinatorial methods, in particular the use of solid phase synthesis methods followed by screening methods in order to arrive at very potent individual compounds, starting from a tool of compounds which include a certain e.g. structural diversity, in a significant shortened time period when compared with the classical synthetic chemistry belongs to the general knowledge of a skilled person. Thus, an inventive step of the present method and use Claims 10,11, 18, 19 and 25-30 cannot be seen.

Claim 24 is directed to a collection in the sense of 'array' or 'library' (see also Section VIII). An unexpected effect of a claimed chemical library itself can be an indication of inventive step. As, however, no unexpected effect is disclosed in the application, the provision of the collections according to Claim 24 appears to be obvious in view of the argumentation set out above.

The representative has brought forward arguments why the claimed object should be considered as inventive, in particular due to the fact that none of the cited document refers to combinatorial methods. These arguments are not persuasive. The basic molecule skeleton is known in compounds with pharmacological activities, see, e.g. D2. In view of the problem underlying the present application, i.e. providing new compounds including the said skeleton it is thus obvious *per se* to use combinatorial methods, in particular solid phase synthesis methods.

4. INDUSTRIAL APPLICABILITY

No objection for Claims 10-27, 29 and 30. For the assessment of the present Claim 28 on the question whether it is industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

VII CERTAIN DEFECTS (DESCRIPTION)

The Applicant has acknowledged several documents, by the term 'incorporated herein by reference'. This gives rise to clarity objections under Art. 6 PCT since it is vague and ambiguous which technical features are referred to. Furthermore, it should be noted that this kind of reference contravenes the basic requirement of each application that the invention must be comprehensible from the specification by itself. In order to overcome the clarity objection, either the phrase 'incorporated by reference' could simply be deleted or the cited prior art under R.5.1(a)(ii) PCT could be discussed in a short summary (see further PCT PRELIMINARY EXAMINATION GUIDELINES PCT/GL/3 MARCH 1993, CHAPTER II, 4.17).

VIII CERTAIN OBSERVATIONS (CLAIMS)

1. Against the representatives opinion, all claims which include the term

'combinatorial unit' are completely unclear in scope. See also Section III (Art. 6 PCT).

2. The scope of Claim 24 is also not clear for the following reasons.
In the field of combinatorial chemistry several expressions are used but not in an unitary sense. A library may denote either a stochastic mixture of potentially active compounds (random library) or a set of spatially separate chemical entities (array). The content of a library is only clear with an indication of the process parameters for its preparation. For example, a library which has been prepared simultaneously in a one pot procedure does not include all species. Due to different reactivities of the reactants some specific compounds are not formed, i.e. the resulting library would not contain any and all possible combinations. Moreover, the use of the term 'collection' alone as in the present case is not limited to those which are prepared by combinatorial methods. The content of the collections claimed is thus completely unclear (Art. 6PCT).
3. Claim 25 is also unclear as the technical features for the preparation are missing.
4. The scope of Claim 30 is also unclear (Art. 6 PCT).

(19) World Intellectual Property Organization
International Bureau



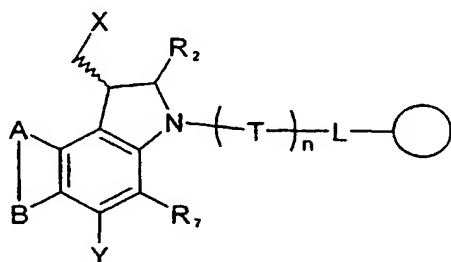
(43) International Publication Date
8 March 2001 (08.03.2001)

PCT

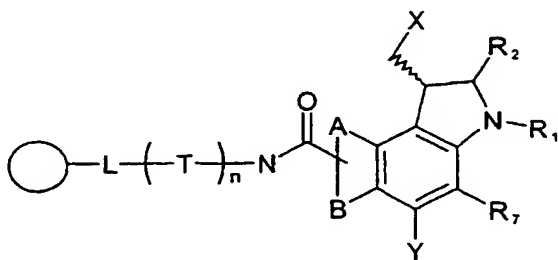
(10) International Publication Number
WO 01/16104 A1

- (51) International Patent Classification⁷: C07D 209/60, A61K 31/404, A61P 43/00, C07D 209/96, C07K 7/02
- (21) International Application Number: PCT/GB00/03291
- (22) International Filing Date: 24 August 2000 (24.08.2000)
- (25) Filing Language: English
- (26) Publication Language: English
- (30) Priority Data:
9920427.3 27 August 1999 (27.08.1999) GB
0005576.4 8 March 2000 (08.03.2000) GB
- (71) Applicant (for all designated States except US):
SPIROGEN LIMITED [GB/GB]; 79 George Street,
Ryde, Isle of Wight PO33 2JF (GB).
- (72) Inventors; and
- (75) Inventors/Applicants (for US only): THURSTON, David, Edwin [GB/GB]; University of Nottingham, Cancer Research Campaign, Experimental Cancer Chemotherapy Laboratories, University Park, Nottingham, Nottinghamshire NG7 2RD (GB). HOWARD, Philip, Wilson [GB/GB]; University of Nottingham, Cancer Research Campaign, Experimental Cancer Chemotherapy Laboratories, University Park, Nottingham, Nottinghamshire NG7 2RD (GB).
- (74) Agents: WATSON, Robert, J. et al.; Mewburn Ellis, York House, 23 Kingsway, London WC2B 6HP (GB).
- (81) Designated States (national): AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW.
- (84) Designated States (regional): ARIPO patent (GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW), Eurasian patent (AM, AZ, BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE), OAPI patent (BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG).
- Published:**
- With international search report.
 - Before the expiration of the time limit for amending the claims and to be republished in the event of receipt of amendments.
- For two-letter codes and other abbreviations, refer to the "Guidance Notes on Codes and Abbreviations" appearing at the beginning of each regular issue of the PCT Gazette.

(54) Title: CYCLOPROPYLINDOLE DERIVATIVES



(III)



(V)

(57) Abstract: Compounds of formula (III) or (V), wherein is a solid support; L is a linking group or a single bond; T is a combinatorial unit; n is a positive integer, where if n is greater than 1, each T may be different; X is an electrophilic leaving group; Y is selected from NH-Prot, O-Prot, S-Prot, NO₂, NHOH, N₃, NHR, NRR, N=NR, N(O)RR, NHSO₂R, N=NPhR, SR or SSR, where Prot represents a protecting group; A and B collectively represent a fused benzene or pyrrole ring (in either orientation), which is optionally substituted by up to respectively 4 or 2 groups independently selected from R, OH, OR, halo, nitro, amino, Me₃Sn, CO₂H, CO₂R; R₁ is a nitrogen protecting group, where if Y includes a protecting group, these protecting groups are orthogonal and R₂ and R₇ are independently selected from H, R, OH, OR, halo, nitro, amino, Me₃Sn, and other related compounds and collections of compounds.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/GB 00/03291

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D209/60 A61K31/404 A61P43/00 C07D209/96 C07K7/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 29642 A (THE SCRIPPS RESEARCH INSTITUTE) 17 June 1999 (1999-06-17) claim 16	1
A	WO 98 11101 A (AUCKLAND DIVISION CANCER SOCIETY OF NEW ZEALAND INC.) 19 March 1998 (1998-03-19) cited in the application claim 1	1
A	WO 97 07097 A (AUCKLAND DIVISION CANCER SOCIETY OF NEW ZEALAND INC.) 27 February 1997 (1997-02-27) claims	1
A	WO 91 16324 A (THE UPJOHN COMPANY) 31 October 1991 (1991-10-31) claims	1



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

8 January 2001

Date of mailing of the international search report

17/01/2001

Name and mailing address of the ISA

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NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Van Bijlen, H

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

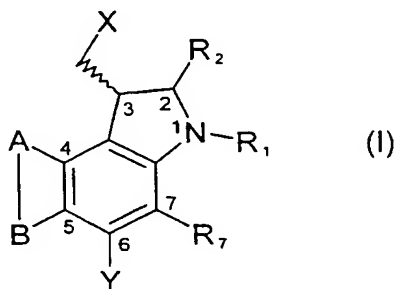
PCT/GB 00/03291

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9929642 A	17-06-1999	AU 1807999 A EP 1037865 A NO 20002900 A	28-06-1999 27-09-2000 08-08-2000
WO 9811101 A	19-03-1998	AU 721037 B AU 4403997 A EP 0938474 A US 6130237 A	22-06-2000 02-04-1998 01-09-1999 10-10-2000
WO 9707097 A	27-02-1997	AU 707644 B AU 6710996 A EP 0850220 A JP 11511113 T NZ 315410 A US 5985909 A	15-07-1999 12-03-1997 01-07-1998 28-09-1999 29-07-1999 16-11-1999
WO 9116324 A	31-10-1991	AU 648313 B AU 7795491 A CA 2078118 A EP 0527189 A JP 5508394 T KR 208957 B KR 209845 B US 5739350 A	21-04-1994 11-11-1991 26-10-1991 17-02-1993 25-11-1993 15-07-1999 15-07-1999 14-04-1998

9. A compound according to any one of the preceding claims, wherein the 4,5 fused ring is substituted by $-\text{CO}_2\text{R}$ in the 2 or 3 position if it is a benzene ring, or in the 2 position if it is a pyrrole ring.

5

10. The use of compounds of formula I:



wherein:

10

X is an electrophilic leaving group;

Y is selected from NH_2 , NH-Prot , OH , O-Prot , SH , S-Prot , NO_2 , NHOH , N_3 , NHR , NRR , N=NR , N(O)RR , NHSO_2R , N=NPhR , SR or SSR , where Prot represents a protecting group;

15

A and B collectively represent a fused benzene or pyrrole ring (in either orientation), which is optionally substituted by up to respectively 4 or 2 groups independently selected from R, OH, OR, halo, nitro, amino, Me_3Sn , CO_2H , CO_2R ;

20

R_1 is a nitrogen protecting group, where if Y includes a protecting group, these protecting groups are orthogonal;

R_2 and R_7 are independently selected from H, R, OH, OR, halo, nitro, amino, Me_3Sn ;

wherein R is selected from:

25

(a) a lower alkyl group having 1 to 10 carbon atoms,

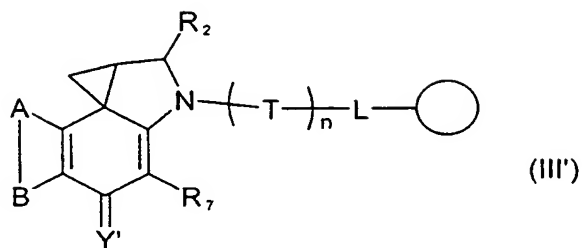
(b) an aralkyl group (i.e. an alkyl group with one or more aryl substituents), preferably of up to 12 carbon atoms;

30

the alkyl group of (a) or (b) optionally containing one or more carbon-carbon double or triple bonds, which may form part of a conjugated system; and

(c) an aryl group, preferably of up to 12 carbon atoms;

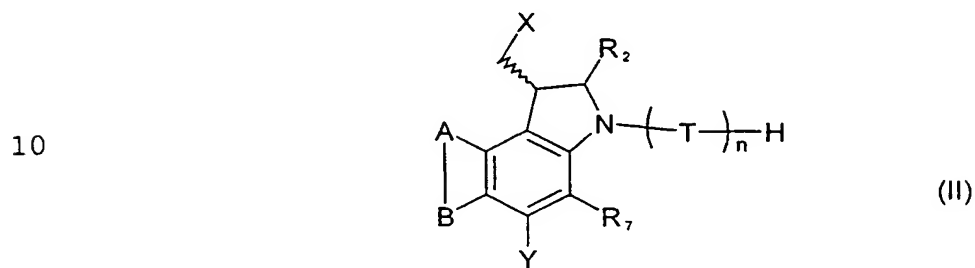
13. A compound of formula **III'**:



wherein:

5 A, B, R₂, R₇, T, n, L and O are as defined in claim 12; and,
Y' is NH, O or S.

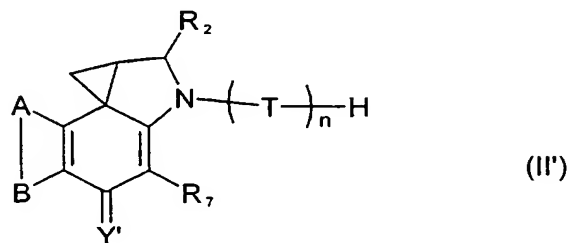
14. A compound of formula **II**:



wherein:

X, Y, A, B, R₂, R₇, T and n are as defined in claim 12.

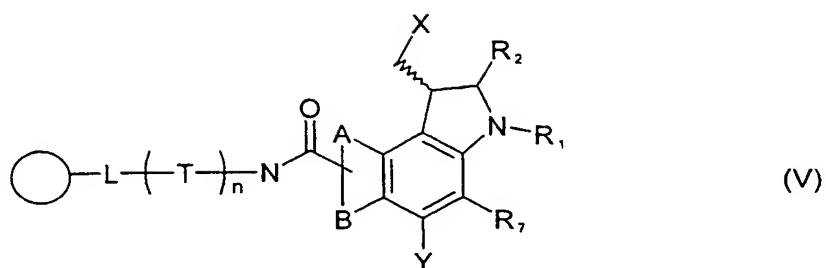
15. A compound of formula **II'**:



wherein:

A, B, T, n, R₂, R₇ and Y' are as defined in claim 13.

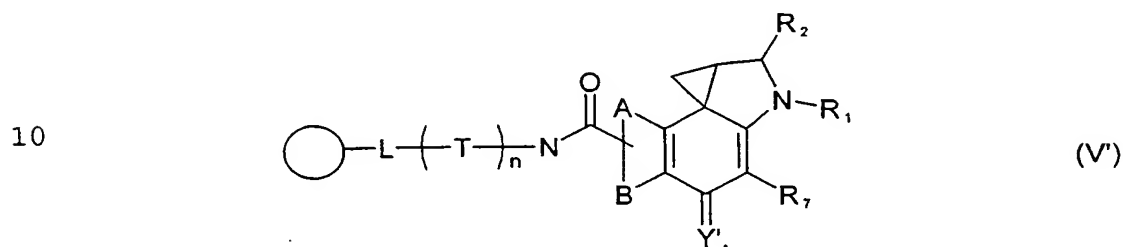
16. A compound of formula V:



wherein:

5 A, B, Y, R_1 , R_2 , and R_7 , are as defined in claim 10; and,
 T, n, L and O are as defined claim 12.

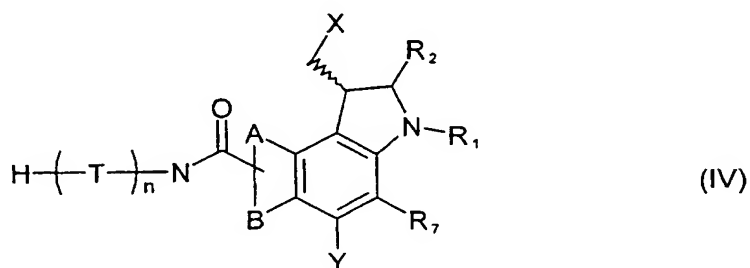
17. A compound of formula V':



wherein:

A, B, R_1 , R_2 , and R_7 are as defined in claim 10; and,
 T, n, L, Y' and O are as defined in claim 13.

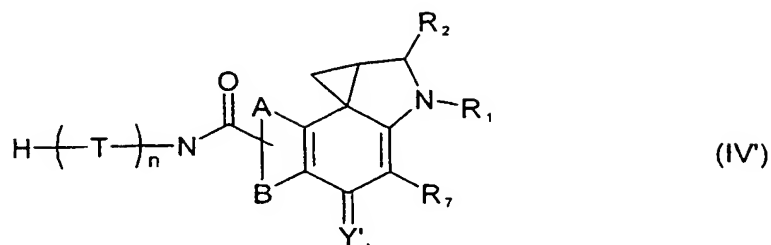
15 18. A compound of formula IV:



wherein:

20 A, B, X, Y, R_1 , R_2 and R_7 are as defined in claim 10; and,
 T and n are as defined in claim 12.

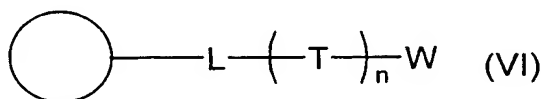
19. A compound of formula IV':



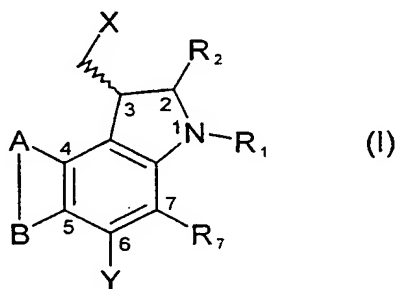
wherein:

A, B, T, n, R₁, R₂ and R₇ are as defined in claim 18; and,
Y' is NH, O or S.

20. A method of preparing a compound according to claim 12 by
reaction of a compound of formula VI:



with a compound of formula I:

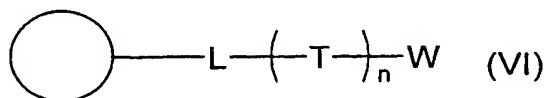


wherein:

A, B, R₂, R₇, T, n, L and O are as defined in claim 12;
and,

W is H or an atom or group for providing a
functional group capable of reaction with -NH₂.

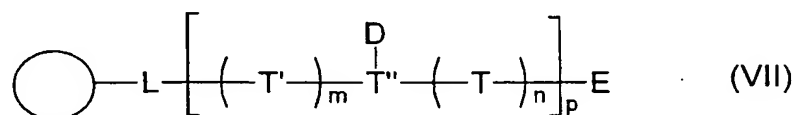
21. A method of preparing a compound according to claim 16, by
reaction of a compound of formula VI:



with a compound of formula I according to claim 10, where the 4,5 fused ring is substituted by $-CO_2R$ in the 2 or 3 position if it is a benzene ring, or in the 2 position if it is a pyrrole ring, and wherein:

- 5 T, n, L and O are as defined in claim 16; and,
 W is H or an atom or group for providing a functional group capable of reaction with $-COOH$.

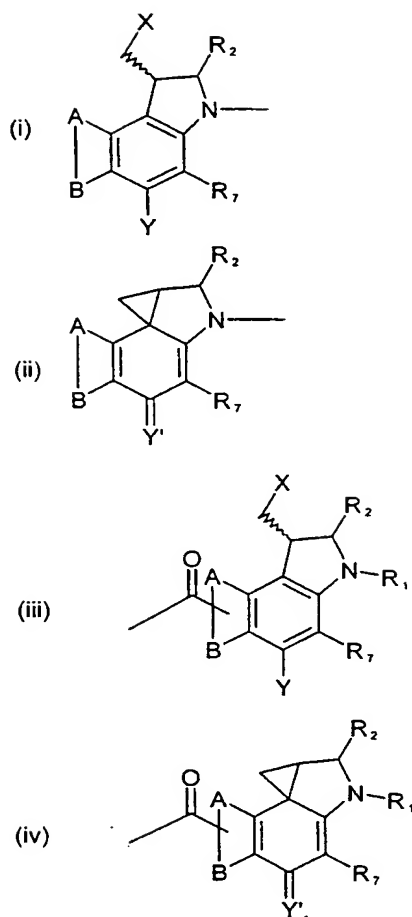
- 10 22. A compound of formula VII:



wherein:

- O, T, and L are as defined in the claim 12;
 n and m are positive integers, or one of them may be
 15 zero;
 T' is a combinatorial unit, where each T' may be different if m is greater than 1;
 T'' is a combinatorial unit which provides a site for the attachment of D;
 20 D is selected from:

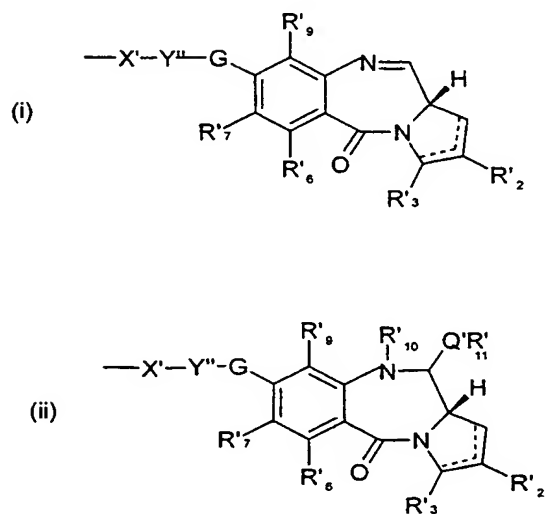
(a)



wherein A, B, Y, R₁, R₂ and R₇ are as defined in claim 11 and Y' is NH, NR, O or S;

5

(b)



wherein:

X' is selected from CO, NH, S, or O;

G is O, S, NH, or a single bond;

R'₂ and R'₃ are independently selected from: H, R, OH, OR, =O, =CH-R, =CH₂, CH₂-CO₂R, CH₂-CO₂H, CH₂-SO₂R, O-SO₂R, CO₂R, COR and CN, and there is optionally a double bond between C₂ and C₃;

R'₆, R'₇, and R'₉ are independently selected from H, R, OH, OR, halo, nitro, amino, Me₃Sn;

R'₁₁ is either H or R;

Q' is S, O or NH;

R'₁₀ is a nitrogen protecting group;

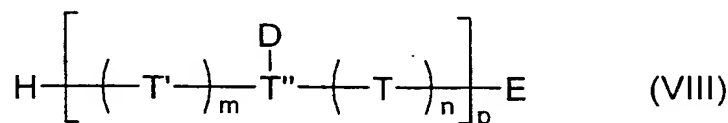
Y'' is a divalent group such that HY = R;

p is a positive integer, where if p is greater than 1, for each repeating unit, the meaning of T, T', T'' and D and the values of n and m are independently selected; and,

E is selected from the same possibilities as D;

provided that at least one group D or E is selected from (a).

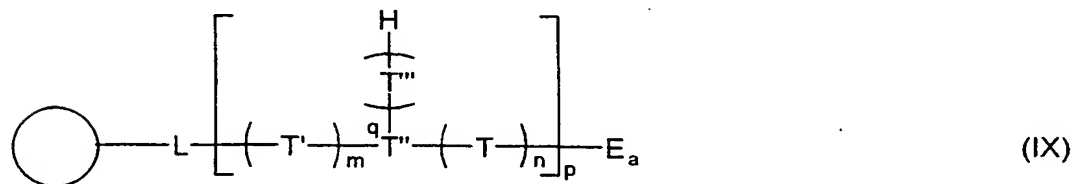
23. A compound of formula (VIII):



wherein:

L, T, T', T'', D, E, n, m and p are as defined in claim 22.

24. A compound of formula (IX):



wherein:

O, L, T, T', T'', n, m and p are as defined in claim 22;

T''' is a combinatorial unit;

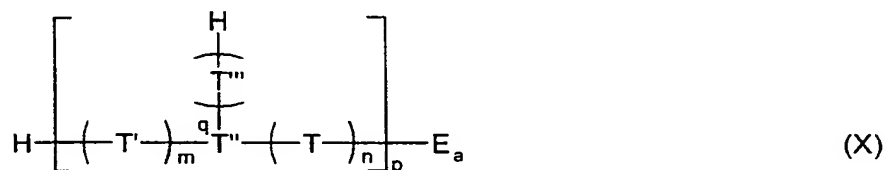
q is a positive integer, where if q is greater than 1,
5 each T''' may be different; and,

E_a is selected from the group (a) of E as defined in
claim 22;

wherein:

10 if p is greater than 1, for each repeating unit the
meaning of T, T', T'', T''' and the values of n, m and q are
independently selected.

25. A compound of formula (X):



wherein:

L, T, T', T'', T''', E_a, n, m, p and q are as defined in claim
24.

20 26. A collection of compounds all of which are represented by
either:

- (i) formula III as defined in claim 12;
- (ii) formula III' as defined in claim 13;
- (iii) formula II as defined in claim 14;
- 25 (iv) formula II' as defined in claim 15;
- (v) formula V as defined in claim 16;
- (vi) formula V' as defined in claim 17;
- (vii) formula IV as defined in claim 18;
- (viii) formula IV' as defined in claim 19;
- 30 (ix) formula VII as defined in claim 22;
- (x) formula VIII as defined in claim 23;
- (xi) formula IX as defined in claim 24; or,
- (xii) formula X as defined in claim 25.

27. A method of preparing a collection of compounds as defined in claim 26.

28. A method of screening compounds of:

- 5 (i) formula **II** as defined in claim 14;
(ii) formula **II'** as defined in claim 15;
(iii) formula **IV** as defined in claim 18;
(iv) formula **IV'** as defined in claim 19;
(v) formula **VIII** as defined in claim 23; or,
10 (vi) formula **X** as defined in claim 25;
to discover biologically active compounds.

29. The use of a compound of:

- 15 (i) formula **II** as defined in claim 14;
(ii) formula **II'** as defined in claim 15;
(iii) formula **IV** as defined in claim 18;
(iv) formula **IV'** as defined in claim 19;
(v) formula **VIII** as defined in claim 23; or
(vi) formula **X** as defined in claim 25;
20 in the manufacture of a cytotoxic, antibiotic, antiparasitic
or antiviral therapeutic composition.

30. The use of a compound of:

- 25 (i) formula **III** as defined in claim 12;
(ii) formula **III'** as defined in claim 13;
(iii) formula **V** as defined in claim 16;
(iv) formula **V'** as defined in claim 17;
(v) formula **VII** as defined in claim 22; or,
(vi) formula **IX** as defined in claim 24;
30 in a method of diagnosis.

31. The use of a compound of:

- 35 (i) formula **II** as defined in claim 14;
(ii) formula **II'** as defined in claim 15;
(iii) formula **IV** as defined in claim 18;
(iv) formula **IV'** as defined in claim 19;
(v) formula **VIII** as defined in claim 23; or,

(vi) formula X as defined in claim 25;
in a method of target validation.

32. The use of a compound of:

- 5 (i) formula II as defined in claim 14;
 (ii) formula II' as defined in claim 15;
 (iii) formula IV as defined in claim 18;
 (iv) formula IV' as defined in claim 19;
 (v) formula VIII as defined in claim 23; or,
10 (vi) formula X as defined in claim 25;
in a method of functional genomics.

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference RJW/LP5871900	FOR FURTHER ACTION <small>see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.</small>	
International application No. PCT/GB 00/03291	International filing date (day/month/year) 24/08/2000	(Earliest) Priority Date (day/month/year) 27/08/1999
Applicant THE UNIVERSITY OF PORTSMOUTH HIGHER EDUCATION CORP		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 2 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

CYCLOPROPYLINDOLE DERIVATIVES

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No. _____

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☐ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

GB 00/03291

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 C07D209/60 A61K31/404 A61P43/00 C07D209/96 C07K7/02

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 C07D A61K A61P C07K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 99 29642 A (THE SCRIPPS RESEARCH INSTITUTE) 17 June 1999 (1999-06-17) claim 16 ---	1
A	WO 98 11101 A (AUCKLAND DIVISION CANCER SOCIETY OF NEW ZEALAND INC.) 19 March 1998 (1998-03-19) cited in the application claim 1 ---	1
A	WO 97 07097 A (AUCKLAND DIVISION CANCER SOCIETY OF NEW ZEALAND INC.) 27 February 1997 (1997-02-27) claims ---	1
A	WO 91 16324 A (THE UPJOHN COMPANY) 31 October 1991 (1991-10-31) claims -----	1

☐ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

° Special categories of cited documents :

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *&* document member of the same patent family

Date of the actual completion of the international search

8 January 2001

Date of mailing of the international search report

17/01/2001

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Authorized officer

Van Bijlen, H

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

P 00/03291

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
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WO 9116324 A	31-10-1991	AU 648313 B AU 7795491 A CA 2078118 A EP 0527189 A JP 5508394 T KR 208957 B KR 209845 B US 5739350 A	21-04-1994 11-11-1991 26-10-1991 17-02-1993 25-11-1993 15-07-1999 15-07-1999 14-04-1998